Daily Oral Care and Cough Reflex Sensitivity in Elderly Nursing Home Patients*

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Background: **Intensive oral care can reduce the incidence of pneumonia in elderly nursing home patients, but the mechanism is unknown.**
Objective: **To explore the effects of intensive oral care on impaired cough reflex sensitivity, which is a known risk factor of aspiration pneumonia.**
Methods: **Cough reflex sensitivity to citric acid was measured in elderly nursing home patients, who were randomly assigned to the intervention group (n = 30) and the control group (n = 29). The patients in the intervention group had their teeth and gingiva cleaned by caregivers after every meal for 1 month. The patients in the control group performed their own oral care during the same period. Serum substance P (SP) concentration, cognitive function, and activities of daily living (ADL) were also assessed.**
Results: **In the intervention group, cough reflex sensitivity at 30 days showed significantly higher sensitivity than baseline ($p < 0.01$). At 30 days, the cough reflex sensitivities in the intervention group were significantly higher than that of the control group ($p < 0.05$). Compared with the control group, the odds ratio of improvement of cough reflex sensitivity was 5.3 (95% confidence interval, 1.7 to 16.0; $p < 0.005$) for the intervention group. One month of intensive oral care did not have a significant effect on serum SP concentration, cognitive function, and ADL.**
Conclusion: **Intensive oral care may reduce the incidence of pneumonia by improving cough reflex sensitivity in elderly nursing home patients.** ***(CHEST 2004; 126:1066–1070)***

Key words: cough reflex; oral care; substance P

Abbreviations: ACE = angiotensin-converting enzyme; ADL = activities of daily living; MMSE = Mini-Mental State Examination; SP = substance P

Impaired cough reflex sensitivity is assumed to play a crucial role in the development of pneumonia in the elderly. A marked depression of cough reflex sensitivity is reported in elderly patients with aspiration pneumonia who revealed cerebral atrophy and lacunar infarction in the brain.[1] The risk of aspiration pneumonia in patients after stroke is known to intimately correlate with the impairment of cough reflex sensitivity.[2,3] Cough reflex sensitivity is impaired in patients after heart-lung transplantation,[4] patients with laryngectomy,[5] and patients with advanced stages of Parkinson disease,[6] who are also highly susceptible to aspiration pneumonia. Recently, it was reported[7] that cough reflex sensitivity was significantly attenuated in patients with recurrent pneumonia who lack apparent underlying illnesses or a predisposition to aspiration. The improvement of cough reflex sensitivity could be a leading preventive strategy for pneumonia in these groups of patients. Heretofore, an angiotensin-converting enzyme (ACE) inhibitor was the only proven way to increase the cough reflex sensitivity and prevent pneumonia in elderly people.[8] However, ACE inhibitors have several limitations. They cannot be used with patients with low BP and a history of vascular edema. Moreover, even with ACE inhibitors, there are patients who fail to restore the cough

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reflex sensitivity. These push us to find another option to restore cough reflex sensitivity in the elderly.

We have reported that intensive oral care lowered the incidence of pneumonia among elderly nursing home patients.[9] Oral care can certainly reduce oropharyngeal colonization with potentially pathogenic organisms. However, since pneumonia in the elderly is a multifactorial phenomenon with no single predominant predictor,[10] we assessed the effect of intensive oral care on cough reflex sensitivity of elderly nursing home patients.

Materials and Methods

Subjects and Study Design

The present study was performed with older patients in a nursing home located near Sendai, Japan. The nursing home has approximately 100 beds and serves as a long-term care facility for older patients who are physically handicapped or suffering from mental deterioration. Thus, to a large extent, they are dependent on the service of caregivers for activities of daily living (ADL). No dentists had been in charge of the institution before the study. The criterion for patient selection was that physical symptoms and cognitive impairment must have been stable for the preceding 3 months. We also excluded patients with chronic pulmonary diseases such as COPD, bronchial asthma, pulmonary fibrosis, and chronic cough. The patients fed themselves or needed help in eating. No patients had feeding tubes. Seventy-six patients met the entry criteria, and we obtained informed consent from 60 patients. Sixty patients were randomly assigned to an intensive oral care (intervention) group or no intensive oral care (control) group in February 2003 using a random-numbers table, and were investigated for 1 month. One patient from the control group was excluded from analysis because he died from stroke before the study finished. Finally, we analyzed 30 patients in the intervention group (13 men; mean age, 87.2 years; range, 70 to 94 years) and 29 patients in the control group (12 men; mean age, 85.0 years; range, 70 to 93 years). Chronic diseases included previous stroke, hypertension, arrhythmia, previous myocardial infarction, and diabetes mellitus. Mental function varied from slight cognitive impairment to dementia.

In the intervention group, during the 1 month, nurses or caregivers cleaned the patients' teeth with a toothbrush for approximately 5 min after each meal. The brushing was performed as a usual daily tooth brushing without dentifrice, including brushing palatal and mandibular mucosa and tongue dorsum. In the control (nonintensive oral care) group, some patients performed their own oral care once a day or irregularly, but none of them requested oral care from caregivers. Twenty-seven patients were totally edentulous and wore full dentures. Three patients still retained some of their own teeth and used partial dentures. Twenty-nine patients retained their own teeth (usually not full) and did not wear dentures. There were no patients who were totally edentulous and did not wear dentures. In both groups, if patients used dentures, whether full or partial, they were cleaned with a denture brush after every meal and with denture cleanser once a week by caregivers. Dentists or dental hygienists administered professional care such as plaque and calculus control as necessary once a week for the intervention group. Both groups were treated with usual nursing management of changing sheets and gowns once a week, sponge bath once a week, and changing diapers as requested.

The cough reflex sensitivity before breakfast was examined before the study and at 3 days, 10 days, and 30 days after the study began. Cognitive impairment was evaluated with the Japanese version of the Mini-Mental State Examination (MMSE), which has a 30-point scale for healthy people, with a score of 0 indicating complete loss of cognitive function.[11] ADL were evaluated using the Barthel index, which has a 100-point scale for independent people, with a score of 0 indicating complete dependence.[12] The serum substance P (SP) concentration before breakfast, and MMSE and ADL scores of each participant were evaluated at the beginning of the study and at 30 days. The protocol was approved by the Tohoku University Ethics Committee. Individual informed consent was obtained from the patients or their family after a detailed explanation of the procedure, but not of the purposes of the study.

Cough Reflex Sensitivity

Cough reflex sensitivity to citric acid was evaluated with a tidal breathing nebulized solution delivered by ultrasonic nebulizer (MU-32; Sharp Company Ltd.; Osaka, Japan).[6] The nebulizer generated particles with a mean mass median diameter of 5.4 μm at an output of 2.2 mL/min. Citric acid was dissolved in saline solution, providing a twofold incremental concentration from 0.7 to 360 mg/mL. Cough was recorded on a Fleisch pneumotachograph (Phipps & Bird; Richmond, VA) mounted at the expiratory ports of the valve. The cough threshold was defined as the concentration at which the patients coughed at least five times during 1 min of breathing the citric acid aerosol. Each nebulizer application had a 2-min interval.

Serum SP Concentration

Blood was collected before evaluating cough reflex sensitivity in a tube containing 0.5 U/mL aprotonin and 3 mmol/L ethylenediamine tetra-acetic acid before breakfast, and was immediately centrifuged to separate serum from cell fraction. The SP was quantified using a modification of a previously described method.[13] For radioimmunoassay, the samples were mixed with two-volume (volume/volume) acetone using a mixer at room temperature for 5 min. The precipitate was pelleted by centrifugation at 2,500*g* for 5 min. After centrifugation, the supernatants were extracted twice with petroleum ether, and the supernatant was then evaporated in a water bath under N_2 gas. After evaporation, the dried residue was dissolved in a 0.05 mol/L Tris-HCl buffer (pH 8.65) containing 0.1% human serum albumin, 0.01 mol/L ethylenediamine tetra-acetic acid, 0.15 mol/L NaCl, and 0.002% sodium azide; 0.2 mL of samples were incubated with 0.05 mL of rabbit anti-SP serum (SRL Inc.; Tokyo, Japan) for 24 h at 4°C. ^{125}I SP, 15,000 counts per minute (NEN Life Science Products; Boston, MA) in 0.05 mL was added and the mixture incubated for an additional 24 h at 4°C. Bound and free ligands were separated by adding 0.05mol/L Tris-HCl buffer, 1% γ-globulin and 25% polyethyleneglycol (6,000 mol/L), and centrifuged at 1,700*g* for 20 min. The radioactivity in the precipitate was counted with a γ-spectrometer.

Statistics

Values are expressed as mean (SE). Data are transformed to logarithmic values for the cough reflex threshold. Comparison of the cough reflex threshold between the groups over the time course was performed by two-way, repeated-measures analysis of variance. Comparison of the cough reflex threshold between the groups at each time point such as baseline, 3 days, 10 days, and 30 days after the study began was performed by the Mann-

Whitney *U* test. One-way analysis of variance for repeated measurements with Fisher least significant difference as a *post hoc* test was used to test the difference in the cough reflex threshold over time within a group. Comparisons between control and intervention groups for age, serum SP, MMSE, and ADL at baseline were evaluated by the Mann-Whitney *U* test. Comparisons between baseline and 30 days after the study began within the group for serum SP, MMSE, and ADL were done by the Wilcoxon signed-rank test. The χ^2 test was used to estimate the difference in gender or denture usage between control and intervention groups. A Fisher exact test was used to examine the association between intervention or edentate status and improvement of cough reflex; $p < 0.05$ was considered significant.

Results

There were no significant differences in age, gender, and teeth status between the control and the intervention groups (Table 1). At baseline, there were also no significant differences in cough reflex threshold (1.4 log mg/mL [SE, 0.1] vs 1.5 log mg/mL [SE, 0.1]), serum SP concentration, MMSE score, and ADL score between the control group and the intervention group (Table 2). When the change of cough reflex sensitivity over time was compared between the control and intervention groups, two-way, repeated-measures analysis of variance revealed a differential changing pattern between the groups ($p < 0.05$) [Fig 1]. There was no significant difference in cough reflex sensitivities among the time points in the control group. In contrast, in the intervention group, the cough reflex threshold at 30 days showed significantly lower values than baseline ($p < 0.01$) and 3 days after the study began ($p < 0.005$). In a comparison between the groups at each time point, the cough reflex threshold did not show a significant difference at 3 days and 10 days, whereas at 30 days, the cough reflex threshold in the intervention group was significantly lower than that of the control group ($p < 0.05$). Compared with the control group, the odds ratio of improvement of cough reflex sensitivity was 5.3 (95% confidence interval, 1.7 to 16.0; $p < 0.005$ by Fisher exact test) for the intervention group. However, 1 month of intensive oral care did not have a significant effect on serum SP concentration, MMSE score, and ADL score (Table 2).

Since only those with their own teeth could have any periodontal disease and such individuals may be more likely to benefit from oral care, we investigated whether the effects of intensive oral care was any different in those with their own teeth (n = 16) as compared to edentulous individuals (n = 14). However, compared with edentulous individuals, there

Table 1—*Age, Gender, and Denture Status of Patients**

Variables	Control Group (n = 29)	Intervention Group (n = 30)	p Value
Age, yr	87.2 (SE 0.9)	85.0 (SE 1.6)	0.16†
Gender, No.			
Male	12	13	0.88‡
Female	17	17	
Denture use, No.*			
Full	13	14	0.30‡
Partial	1	2	
No	15	14	

*Full denotes the patients who were totally edentulous and wore full dentures. Partial denotes the patients who still retained some of their own teeth and used partial dentures. No denotes the patients who still retained their own teeth and did not use dentures.
†Estimated by Mann-Whitney *U* test.
‡Estimated by χ^2 test.

Table 2—*Effect of Intensive Oral Care on Serum SP Concentration, MMSE Score, and ADL Score in Elderly Nursing Home Patients**

Variables	Control Group (n = 29)		Intervention Group (n = 30)	
	Baseline	30 Days	Baseline	30 Days
Serum SP, pg/mL	15.3 (1.2)	15.4 (1.0)	15.1 (1.2)	15.7 (1.6)
MMSE score	13.8 (1.9)	13.6 (1.8)	12.8 (1.7)	13.7 (1.8)
ADL score	45.7 (7.1)	47.1 (7.5)	45.1 (7.1)	44.4 (7.2)

*Values are expressed as mean (SE). There was no significant difference between control and intervention groups for all items both at baseline and 30 days (Mann-Whitney *U* test). There was also no significant difference between baseline and 30 days after the study began within the group for all items (Wilcoxon signed-rank test).

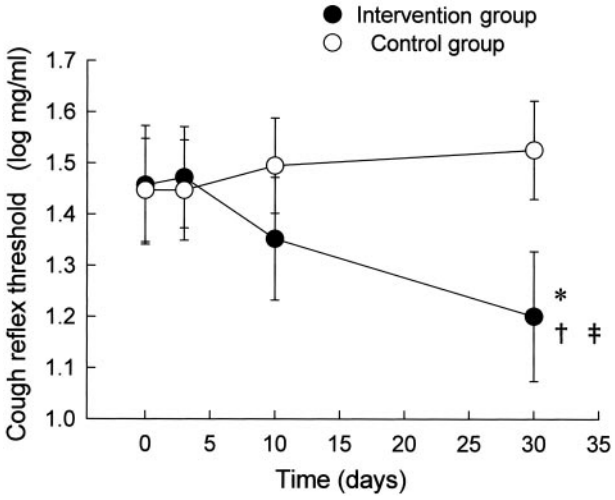

Figure 1. Cough reflex threshold in elderly nursing home patients treated with intensive oral care (the intervention group, n = 30; closed circle) and without intensive oral care (the control group, n = 29; open circle) during the follow-up period. Values are expressed as mean (SE). *$p < 0.05$ vs the control group at 30 days. †$p < 0.01$ vs the intervention group at 0 days (baseline). ‡$p < 0.005$ vs the intervention group at 3 days.

was no significant difference in the improvement of cough reflex sensitivity in patients with their own teeth (odds ratio, 2.25; 95% confidence interval, 0.6 to 10.6).

Discussion

In this study, we showed that intensive oral care can improve cough reflex sensitivity in elderly nursing home patients. The cough reflex thresholds in healthy older people who lead an active daily life were reported to be < 1 log mg/mL.[14] Cough reflex sensitivity at baseline for our patients was moderately impaired and was near the borderline (1.35 log mg/mL) of high risk for acquiring pneumonia within the following year.[3] Therefore, it is of clinical importance to improve cough reflex sensitivity in this population. Previously, we reported that intensive oral care improved dysphagia due to restoring the swallowing reflex in the elderly.[15] Dysphagia is an important risk for aspiration pneumonia, but generally not sufficient to cause pneumonia unless other risk factors are present.[2,3,10] The patients receiving intensive oral care had fewer incidences of pneumonia than did elderly patients not receiving oral care in nursing homes.[9] Intensive oral care may reduce the incidence of pneumonia by not only reducing oropharyngeal colonization but also by improving both swallowing and cough reflex sensitivities.

Different from our previous study,[15] we failed to show an improvement of ADL with 1 month of intensive oral care. This might be explained by relatively lower ADL in the present study. We also failed to show the elevation of serum SP concentration, whereas our previous study[15] showed that salivary SP concentration was elevated by 1 month of intensive oral care. Since SP is the neurotransmitter that is believed to play a major role in both cough and swallowing sensory pathways,[16,17] the improvement of cough and swallowing reflex was theoretically expected to be related to the elevation of SP. Systemic SP concentration may not reflect locally elevated SP because of the ubiquitous breakdown pathways of SP. Although the SP concentration of hypertonic saline-induced sputum could be a better indicator of elevated SP in the respiratory sensory system,[6] it was difficult to obtain from our patients due to low cognitive and functional status.

The mechanism of improvement of cough reflex sensitivity by intensive oral care is unclear. It is possible that the long-term exposure to oropharyngeal microbial pathogens introduced into the lower respiratory tract by silent aspiration may desensitize cough receptors residing within airway epithelium, whether structurally or functionally. Long-term microaspiration may change mucus thickness and composition, or may deplete neuropeptides in nerve endings, as seen in smokers.[18,19] Intensive oral care may relieve desensitization of the cough receptor by reducing the chance of exposure to oropharyngeal microbial pathogens. Another explanation, which seems to be more likely for us, is that stimulation of oral sensory nerves by intensive oral care may activate the CNS that is related to the cough reflex. A 2-year follow-up on intensive oral care showed a tendency of improvement of ADL and cognitive functions.[9] Since our knowledge about central control mechanisms of cough reflex is still seriously scanty, further studies are needed to clarify the relationship between oropharyngeal mechanical stimulation and cough reflex sensitivity, as well as ADL and cognitive functions.

Our study suggests that intensive oral care may prevent aspiration pneumonia in elderly nursing home patients, at least in part by improving cough reflex sensitivity. Cough reflex sensitivity was blunted in not only elderly patients in the nursing home but also in patients after heart-lung transplantation,[4] patients after laryngectomy,[5] patients with advanced stages of Parkinson disease,[6] and patients with recurrent pneumonia who lack apparent underlying illnesses or a predisposition to aspiration.[7] Fatal aspiration pneumonia is intimately correlated with the impairment of cough reflex sensitivity in these patients. Since the way to restore the cough reflex sensitivity is seriously limited, it is of importance to investigate whether intensive oral care can improve the cough reflex sensitivity in these patients.

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